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ABSTRACT

AN EPIDEMIOLOGIC INVESTIGATION OF PULMONARY FUNCTION AND RESPIRATORY SYMPTOMS AMONG TOLUENE DIISOCYANATE PRODUCTION PLANT EMPLOYEES

Irrelevant, internal codes

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The Texas Division of Dow Chemical U.S.A. has manufactured Toluene Diisocyanate (TDI) since 1976. Recent studies of pulmonary function changes among workers of TDI manufacturing plants of other companies have suggested that significant declines of lung function may occur due to exposures below the current TDI OSHA ceiling standard of 20 ppb. We propose a cross-sectional study to determine if depressed pulmonary function is observed in Texas Division TDI manufacturing employees. Pulmonary function tests will be performed on all current TDI personnel as well as personnel from a department without any known respiratory irritants. A detailed respiratory questionnaire inquiring about smoking status and atopy as well as exposures will be administered to all study subjects. Comparisons of FVC, FEV₁ and prevalence of respiratory symptoms between the study and comparison group will be done. Duration and rank level of exposure will be regressed against the absolute difference between observed and predicted results to test for dose response. Analysis of this data will help to determine the prevalence of respiratory symptoms and lung function as they relate to length of exposure, atopy, smoking patterns and level of presumptive exposure in a TDI manufacturing plant.

INTRODUCTION

Three distinct types of respiratory effects have been reported to follow exposure to toluene diisocyanate (TDI) vapors.¹ At high concentrations (above 500 ppb), there is a direct toxic effect which produces acute inflammation of the conjunctivae and mucous membranes of the upper and lower respiratory tracts. Asthma in specifically sensitized employees may occur at much lower concentrations due to a presumed hypersensitivity reaction. Finally, there is conflicting evidence that chronic exposure may result in the development of fixed chronic obstructive airway disease.

Adams studied 180 asymptomatic TDI production employees for up to 9 years and reported no evidence of chronic ventilatory impairment due to exposure.² Peters and colleagues³⁻⁵ and Wegman et al.^{6,7} studied polyurethane workers and suggested that chronic exposure to TDI at levels below the current OSHA ceiling standard of 20 ppb was responsible for a marked excess annual decline in ventilatory function. More recently, Weill et al.⁸ conducted a five-year longitudinal study of 223 workers in a new TDI manufacturing plant and concluded that the effects observed in their study support the NIOSH-recommended standard of 5 ppb TDI as an 8-hour TWA.

The Texas Division of Dow Chemical U.S.A. has manufactured TDI for use in VORANATE^{*} rigid urethane foams since 1976, and thus, has an exposed workforce. In response to a request from the Texas Division Industrial Medicine Department, we propose to conduct a cross-sectional epidemiologic investigation. Data on lung function and prevalence of respiratory symptoms, as well as other host factors will be collected as part of the yearly periodic health exam. Analysis of these data will help determine the prevalence of respiratory symptoms and lung function as they relate to length of exposure, atopy, smoking patterns and level of exposure.

Contingent on the findings of this study, a prospective longitudinal study be warranted. It would be designed to address the question concerning acute and long-term exposures and their associations with decrements in lung function. This further investigation would be dependent on the development of analytical techniques to effectively measure TDI levels on a short-term as well as a long-term basis.

*Trademark of The Dow Chemical Company

LITERATURE REVIEW

Chronic Obstructive Lung Disease

Chronic obstructive lung disease (C.O.L.D.) is an important cause of death and an even greater cause of disability. Approximately 25,000 deaths each year in the United States are directly attributable to chronic bronchitis, emphysema and asthma. Many more premature deaths, from complications associated with infection and cardiac failure, have an underlying respiratory disease which contributes. The disease is more common among men and its incidence increases rapidly with age.

The diagnosis of C.O.L.D. is usually made on the basis of symptomatology and measurement of vital capacity (spirometry). For the purposes of epidemiologic study, disease assessment is usually made using a respiratory questionnaire and from spirometry. Of the various lung function parameters, the forced expiratory flow rate at between 25% and 75% of total vital capacity (FEF25-75) is probably the most sensitive indicator of disease, but has the most variability.⁹ The forced expiratory volume in one second is less sensitive, but is more stable and is most frequently employed. Total vital capacity (FVC) is the least sensitive indicator.

Without a doubt, cigarette smoking has been found to be the most important cause of chronic respiratory disease. Even so, only a fraction of smokers are affected severely enough to become

disabled by it. Smoking appears to cause a more rapid loss of FEV with advancing age. If smokers quit their habit, their lost FEV is not totally regained, but the rate of loss returns to normal.

Occupational exposure to certain dusts, gases, mists or fumes can contribute to the development of C.O.L.D. Acute incidents of severe air pollution have also been linked to increased morbidity and mortality from this disease. The disease has been found to be more common among the lower socioeconomic groups but this has been attributed to heavier smoking.

Studies of the Effects of Exposure to TDI

Case reports of the direct toxic effects of high exposures to TDI and of its ability to induce a sensitivity reaction in some individuals are summarized elsewhere.¹⁰ Of prime interest to the questions at hand are the studies done since the early 1960's to detect changes in pulmonary function attributable to chronic TDI exposure. These studies have produced somewhat conflicting results.

In 1963, Gandevia reported on acute changes in FEV_1 occurring among employees engaged in manufacturing rigid polyurethane foam.¹¹ Concentrations of TDI were estimated at 900 ppb. Fifteen of the 20 men employed were available for testing and, over a three week period, they experienced a significant decrease in FEV_1 of 0.227 liter; the mean diurnal decrease of 0.18 liter during a normal

working day was also significant. The authors noted that values determined on Friday morning were significantly lower than those on Monday, indicating that the effects were cumulative and complete recovery did not occur overnight.

Williamson followed changes in pulmonary function over a 14 month period among 15 workers in an operation where TDI was separated from a solvent by distillation.¹² Concentrations of TDI were all above 20 ppb. The author observed four series of measurements of FVC and FEV_1 and noted no significant change from baseline values, except a fall in FEV_1 at the time of the second measurement. There was little difference between Monday and Friday values; daily changes were not measured.

Peters et al examined thirty-eight workers exposed to levels of TDI below 20 ppb at the beginning and end of a workday after a weekend of no exposure.³ These employees were engaged in the manufacture of polyurethane foam. Statistically significant decreases occurred in FVC, FEV_1 , peak flow rate, and expiratory flow rates at 50% and 25% of vital capacity. Thirty-four of these same workers were examined Friday and it was found that the FVC had returned to baseline, the FEV_1 was still depressed and the expiratory flow rates were more depressed. Diurnal variation could not account for these changes. Workers with respiratory symptoms showed greater decreases in FEV_1 than workers without symptoms.

Peters et al repeated their measurements of ventilatory capacity, in the same factory and on the same workers, six months later.⁴ The study was conducted to determine whether TDI caused any cumulative or chronic effect on ventilatory capacity and whether sensitive individuals could be predicted. The tests of pulmonary function were conducted on Monday morning and afternoon, and on Tuesday morning and afternoon. Twenty-eight of the 34 workers included had been examined six months earlier. On Monday a mean decline in FEV_1 of 0.16 liter occurred that did not return to baseline value (Monday A.M.) on Tuesday morning. The FEV_1 fell an average of 0.14 liters over the six-month period and flow rates at 75%, 50%, 25%, and 10% of vital capacity also decreased significantly. There was a highly significant correlation coefficient ($r = 0.72$) between one-day changes in FEV_1 and six-month changes in FEV_1 . Workers with respiratory symptoms demonstrated greater falls in FEV_1 than did asymptomatic workers. The authors felt these latter two observations might be useful for detecting workers likely to be affected by exposure to TDI.

Twelve months of additional follow-up on these same workers was summarized by Peters and colleagues in 1970.⁵ There were 25 and 19 workers common to the first and third (12 months) surveys and first and fourth (18 months) surveys, respectively. Although there was no change observed between the second and third survey, the decline observed between the third and fourth surveys was consistent with the change noted in the first six months. The authors concluded that there were cumulative changes in ventilatory

capacity observed among workers exposed to TDI at levels below 20 ppb during the 18 months of the study.

Adams studied annual decline in pulmonary function among 180 asymptomatic workers engaged in the production of TDI in England.² Results during 1964-1972 were compared with values of 608 control subjects living nearby who had no contact with TDI. Results from the standard Medical Research Council (MRC) respiratory questionnaire given to 76 men still employed at the plants were compared with those from 76 controls who had no contact with TDI, but who did similar work at a nearby chemical plant. Prior to 1965, airborne concentrations of TDI frequently exceeded 20 ppb; but after this date, the exposures were generally below this level.

Comparison of pulmonary function data from the 180 exposed with those of the 608 controls revealed that TDI did not affect their FEV₁ or FVC values. No significant differences in prevalence of respiratory symptoms were found between 76 currently employed men exposed to TDI and controls. Adams followed-up sensitized workers no longer exposed to TDI and found that they had more respiratory symptoms than did unexposed controls, suggesting that long term effects do occur in some individuals developing acute symptoms after TDI exposure.

Wegman et al performed pulmonary function testing on 112 workers exposed to TDI during manufacture of polyurethane cushions.⁶ Results from the MRC respiratory symptom questionnaire

were collected and FEV₁ was measured pre- and post-shift on a Monday following a three-day weekend. Employees were divided into three exposure groups: 1.5 ppb, 2.0 - 3.0 ppb, and 3.5 ppb. A dose-related diurnal decrease in FEV₁ was found in the three groups. The total group was examined two years later and only 63 original members were still employed.⁷ Fifty-seven members could be assigned to one of three exposure groups on the basis of usual work station. Two-year decreases in FEV₁ of 0.012, 0.085 and 0.205 liter were noted in the 1.5 ppb, 2.0-3.0 and 3.5 ppb exposure groups, respectively. Age, length of employment, and smoking habits did not differ significantly in the three groups. The authors concluded that an excessive loss of lung function resulted from exposure to TDI at concentrations at least as low as 3.5 ppb and possibly as low as 2.0 ppb.

These findings contradict those of Adams,² and Wegman et al have offered several possible explanations for this. Adams used area monitoring data to determine TDI concentrations; he considered all subjects equally exposed; all lung function testing was done after a day of exposure, so no baseline data were available; and regression analysis, a less sensitive indicator of changes over time, was used to evaluate changes in lung function. Another explanation for the different findings has been offered: Adams studied workers in TDI-manufacturing plants, whereas, Wegman et al studied workers producing polyurethane cushions.¹⁰ Exposure to other chemicals occurred in both situations and may have affected results of lung function studies. Still another explanation may be

the quality of lung function data gathered by Wegman. Unlike Adams, he did not include a concurrent control group, so the amount of change attributable to variability in testing, cannot be assessed.

Weill et al recently have conducted a five-year multidisciplinary longitudinal study of 223 employees in a new TDI manufacturing plant.⁸ An association was found between higher exposures to TDI and larger annual declines in FEV_1 and FEF_{25-75} . Detailed analysis of FEV_1 annual decline among never smokers, by cumulative TDI exposure category and smoking category, revealed a 38 ml/yr larger average decline in the higher TDI exposure category than in the lower exposure category. Although annual declines in FEV_1 in this population were found to be related to TDI exposure, the magnitudes of mean declines were not large in comparison with those derived in published cross-sectional studies. Conclusions were reached which were different from those of Adams, and methodologic differences may account for this. Adams did not compute individual annual declines nor did he attempt to correlate these with level of TDI exposure. Weill and colleagues did not observe declines of the magnitude observed by Peters et al and Wegman and co-workers. The authors suggested that studies by these latter two groups were plagued by high attrition rates, and were somewhat enigmatic because of a failure to observe a relationship between smoking and FEV_1 annual decline or between length of TDI exposure and initial FEV_1 .¹

Musk et al¹³ have conducted pulmonary function testing on employees exposed to TDI and MDI (diphenyl methane isocyanate) during the manufacture of polyurethane components for automobiles. Two-hundred-and-fifty-nine subjects from three different sites of one manufacturing facility were examined in 1971, and 107 of the subjects were available for re-examination in 1976. They were studied as they arrived at work on a Monday morning, after a weekend of no exposure, and again that afternoon. They were re-examined on the Monday morning following a two-week period when over one-half of them were on vacation, and again on that afternoon.

Airborne concentrations of TDI and MDI were quite low with 90% of samples having been below 0.005 ppm. Bronchitis was found to be more prevalent in cigarette smokers, but there was no association between bronchitis or dyspnea and exposure to isocyanates. The annual decline in FEV_1 was found to be 0.02 liter which the authors judged to be approximately that expected due to ageing alone. The authors felt there was no evidence of selection among those lost-to-follow-up, as those leaving had similar lung function to those who remained. No acute change in FEV_1 could be demonstrated over the course of a Monday, either before or after a two-week vacation. No improvement in ventilatory function was observed over the vacation period. It was concluded that isocyanate exposure can be controlled to the point of eliminating effects as measured by these techniques.

Although the above investigations attempt to relate lung function studies to specific levels of TDI exposure, their results must be interpreted with the knowledge of the limitations of their monitoring methods. Paper tape sampling, as used by Weill and Diem, has a sensitivity at the 5 ppb level of \pm 3-4 ppb.¹⁴ Because of the 3-4 ppb variation it is virtually impossible to assign exact levels below 10 ppb using this method. Colorimetric methods of sample collection using the Marcali¹⁵ method of analysis have a detection range of 0.007 ppm to 0.14 ppm using a 20 liter air sample, but the method accuracy and precision are unknown.¹⁶

METHODS AND MATERIALS

Study Design

A retrospective longitudinal study would be the most efficient approach to establish whether or not chronic exposure to TDI among Texas Division employees has contributed to a greater than expected loss in lung function. This is because maximum use is made of data gathered previously. Unfortunately, a recent change in spirometric equipment prohibits using data obtained prior to August of 1980. Additionally, spirometry data are not available from consecutive years for a suitable unexposed comparison group. For these reasons, a retrospective study is not feasible.

Prospective longitudinal studies have the ability to define temporal relationships between exposure and disease outcome and can

determine the incidence of disease. While this would be a desirable approach to answer this question, it too has its disadvantages. The primary disadvantage of a longitudinal study is the length of time required to adequately follow the study population. This would prove costly and would not provide a timely assessment to the pulmonary function of the exposed population. To adequately characterize exposures on a prospective basis, it would be desirable to measure excursions as well as chronic exposures. The methodology for these types of sampling methods have not yet been refined. Therefore, to address the question as to whether or not employees of the TDI plant have a higher prevalence of respiratory symptoms and decreased lung function, a cross-sectional design was chosen.

Pulmonary function testing is done in the Industrial Medicine Department with an Ohio Medical Spirometer, Model 822. Spirometry is done standing or sitting and noseclips are not used. Three satisfactory forced expiratory maneuvers are performed, and calculations of FEV_1 and FVC are done, corrected to body temperature saturated with water vapor (B.T.P.S.), automatically with a Spirotech microprocessor. A comparison with a predicted value adjusted for age and height is made using Knudson's regression equations.¹⁷ Only data from the best effort in each testing session will be used for statistical analyses. Quality control in pulmonary function testing is critical if meaningful analysis of data is to be done. Such a quality control program

would at a minimum have to meet the criteria outlined recently by Gondek.¹⁸

TDI plant employees who will receive the periodic medical surveillance examination in 1983, will be identified from personnel rosters. Because this examination is voluntary, only data from participants are available for study. To ensure representative findings, participation will be strongly encouraged. Comparisons of duration of plant experience and level of potential exposure between participants and non-participants will be done in order to discern a possible selection bias. All TDI employees (as well as the comparison group) will be scheduled for their exam after at least two days away from work. This will help to diminish the chances of observing effects due to acute exposures.

To determine the prevalence of respiratory symptoms, smoking habit, and atopic status, a special questionnaire (see Appendix A) will be administered to subjects by a qualified person from the medical department at the time pulmonary function testing is done. This questionnaire was used by Weill et al.,⁸ and is a modification of the one developed by the Medical Research Council. While subjects will have completed respiratory health questions as part of the routine periodic medical surveillance examination, the MRC-based instrument is more comprehensive. The prevalence of respiratory symptoms will then be compared between the exposed and the unexposed, stratified on pertinent covariables.

Although there are data available for general or working populations to derive an expected value for vital capacity, it is strongly recommended that a set of concurrent control subjects be selected. Differences in testing procedures and equipment can introduce artificial variability. Ideally, this comparison group should not have had exposure to TDI or to other known respiratory irritants. Employees of the Light Hydrocarbon Plants 6 and 7 have little opportunity for exposure to respiratory hazards and, thus, are judged to be a suitable comparison group. Individuals from these plants who, by virtue of previous work assignments at Dow, have had exposure to known respiratory irritants, will be excluded from consideration as controls. Eligible employees will be scheduled for participation in the medical surveillance examination in 1983.

Individuals for study will be characterized in terms of age, race, sex, height, atopic status, smoking habit, duration and level of potential exposure. Available industrial hygiene survey data will be used to ordinally rank job classifications by level of exposure. (Appendix B).

Although four different ventilatory measurements are made during the expirograms given at the Texas Division Medical Department, only two will be analyzed for differences, FEV_1 , and FVC. These measurements were chosen for analysis for three reasons: (1) the majority of prior investigations into the effect of TDI on lung function used these measurements for assessment of

effect, (2) of all the spirometry measurements available, FEV_1 and FVC have been demonstrated to discriminate between those individuals who do or do not have chronic respiratory symptoms,⁹ (3) while other ventilatory measurements may be more sensitive, they lack the reproducibility and discrimination of FEV_1 and FVC.

A direct comparison of lung function results between the exposed and unexposed may not be possible because of the age and height dependency of results, and because of possible differences between the two groups with respect to the distribution of these variables. As an alternative, it is proposed that the individual measurements in the groups be compared to the predicted values from regression equations derived from general population values. The absolute difference between observed and predicted should be normally distributed about a mean value for the two groups, and a test of the difference between means and variances will be done.²⁰ Duration and level of exposure will then be regressed against absolute difference between observed and predicted to test for dose-response.

Prevalence of respiratory symptoms between the study and unexposed groups will be compared, stratified on pertinent variables.

RATIONALE FOR INTERPRETATION

Recent studies of employees of companies other than Dow exposed to TDI suggest that declines in lung function may be occurring at exposures below the current OSHA ceiling standard of 20 ppb.^{3,4} The Texas Division of Dow Chemical U.S.A. has an exposed workforce which should be evaluated for lung function changes. A cross-sectional study design is proposed to determine if differences in lung function and the prevalence of respiratory symptoms exist between the TDI exposed population and an unexposed group.

This study may have limited statistical power to detect differences in vital capacity between the exposed and unexposed groups as significant. Berry has calculated that a cross-sectional study would require 89 subjects with a mean length of follow-up (time since initial exposure) of 7 years to detect a difference of 30 ml/yr at a significance level of 0.05 and power 0.8.¹⁹ It is unlikely, since the TDI plant opened only 7 years ago, that this study will have available such a sample size. As a consequence, the study will not be able to detect differences as small as 30 ml/yr.

Potential confounding due to host factors will be controlled by stratification. By the use of industrial hygiene data, every attempt will be made to divide plant employees into meaningful exposure groups, and examination for dose-response relationships

will increase the power to detect differences. Employment in the TDI process involves potential exposure to other respiratory irritants, most notably phosgene. It may not be possible to separate those effects attributable to TDI from those attributable to other exposures. This has been a limitation of previous studies as well.

While cross-sectional studies can evaluate the prevalence of disease, they are not able to establish temporal relationships between exposures and the onset of the disease. In this analysis, determination can be made as to whether TDI employees differ from a comparison group in lung function and respiratory symptoms. If such differences are found, and are considered meaningful, then this investigation may need to be expanded into a longitudinal study. The data collected at this time could be used as the first "point" in such a prospective study.

MANPOWER AND BUDGET

Budget estimates represent a "best" guess of time required of investigators and do not include costs of administering lung function tests, industrial hygiene measurements, or of missed work by study participants.

	Time	Recharge Rate	Cost
G. G. Bond	40 hours	<i>Irrelevant, cost data</i>	
R. E. Flake	80 hours		
G. H. Flores	60 hours		
R. R. Cook	20 hours		
W. A. Fishbeck	20 hours		
R. J. Shellenberger	160 hours		

TOTAL

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A P P E N D I X A
TDI STUDY QUESTIONNAIRE

IDENTIFICATION

1. Study Number _____
 2. Master Number _____
 3. Name _____
 4. Date of Birth ____/____/____
 5. Age _____
 6. Race _____
 7. Sex _____
 8. Height _____
 9. Weight _____
-

Acute Exposure Experience

1. Have you had any reaction to a gas exposure in the last six months?

Yes 1 No 2

Note any entry in Acute Exposure File _____

Source: Weill et al.⁸

A P P E N D I X A

(2)

Data Column	Code Column
<u>COUGH</u>	
1. Do you usually cough first thing in the morning in bad weather?	1-4 _____
Yes <u>1</u> No <u>2</u>	5 _____
2. Do you usually cough at other times during the day or at night in bad weather?	6 _____
Yes <u>1</u> No <u>2</u>	
<u>If "yes" to 1 or 2</u>	
3. Do you cough on most days for as much as 3 months of the year?	7 _____
Yes <u>1</u> No <u>2</u> N.A. <u>9</u>	
4. For how many years have you had this cough?	
Less than 2 years <u>1</u>	
2 to 5 years <u>2</u>	
5 years or more <u>3</u>	
N.A. <u>9</u>	8 _____

SPUTUM

1. Do you usually bring up phlegm, sputum or mucous from your chest first thing in the morning in bad weather?	9 _____
Yes <u>1</u> No <u>2</u>	
2. Do you usually bring up phlegm, sputum or mucous from your chest at any other times during the day or night in bad weather?	10 _____
Yes <u>1</u> No <u>2</u>	
<u>If "yes" to 1 or 2</u>	
3. Do you bring up phlegm, sputum or mucous from your chest on most days for as much as 3 months of the year?	11 _____
Yes <u>1</u> No <u>2</u> N.A. <u>9</u>	

APPENDIX A

(3)

Data Column	Code Column
4. For how many years have you raised phlegm, sputum or mucous from your chest?	
Less than 2 years	<u>1</u>
2 to 5 years	<u>2</u>
5 years or more	<u>3</u>
N.A.	<u>9</u>
	12 __

WHEEZING

1. Does your breathing ever sound wheezy or whistling?

Yes 1 No 2 13 __

2. Have you ever had attacks of shortness of breath with wheezing?

Yes 1 No 2 14 __

If "yes" to 1

3. For how many years has your breathing sounded wheezy or whistling?

__ __ N.A. 9 9 15-16 __ __

If "yes" to 2

4. Do you have attacks of shortness of breath with wheezing at present?

Yes 1 No 2 N.A. 9 17 __

BREATHLESSNESS

1. Are you troubled by shortness of breath when hurrying on level ground or walking up a slight hill?

Yes 1 No 2 18 __

(4)

Data Column	Code Column
2. Do you get short of breath when walking with other people your own age on level ground?	
Yes <u>1</u> No <u>2</u>	19 <u> </u>
<u>If "yes" to 1 or 2</u>	
3. For how many years have you had shortness of breath?	
<u> </u> <u> </u> N.A. <u>9</u> <u>9</u>	20-21 <u> </u> <u> </u>

CHEST ILLNESS

1. During the past 3 years, how much trouble have you had with illnesses such as chest colds, bronchitis or pneumonia?

0 1 2 3 4 5

none great deal

22

2. During the past 3 years, how often were you unable to do your usual activities because of illnesses such as chest colds, bronchitis or pneumonia?

One time	<u>1</u>
2-5 times	<u>2</u>
more than 5 times	3

23

3. Do you think you have ever had any of these chest disorders: asthma, any kind of bronchial trouble, or emphysema?

Yes 1 No 2 D.K. 3

24

4. Has a doctor ever told you that you had asthma, some kind of bronchial trouble, or emphysema?

Yes 1 No 2

25

If "yes" to 4

- | | | | |
|----------------|------|---|----|
| 5. Which type? | N.A. | 9 | 26 |
|----------------|------|---|----|

A P P E N D I X A

(5)

Data Column	Code Column
Have you ever had repeated attacks of pneumonia?	
Yes <u>1</u> No <u>2</u>	27 <u> </u>
Have you ever been hospitalized for	
Pleurisy Yes <u>1</u> No <u>2</u>	28 <u> </u>
Tuberculosis Yes <u>1</u> No <u>2</u>	29 <u> </u>
If "yes" when? <u> </u>	30 <u> </u>

AL CATARRH

Do you usually have a drip at the back of your nose?	
Yes <u>1</u> No <u>2</u>	31 <u> </u>
<u>If "yes" to 1</u>	
Do you have a drip at the back of your nose for as much as three months?	
Yes <u>1</u> No <u>2</u> N.A. <u>9</u>	32 <u> </u>
Have you ever had hay fever?	
Yes <u>1</u> No <u>2</u>	33 <u> </u>
Have you ever had a runny, stuffy or itchy nose and/or sneezing for several days at a time occurring at certain times of the year?	
Yes <u>1</u> No <u>2</u>	34 <u> </u>
Have you ever had sinus trouble or a postnasal drip?	
Yes <u>1</u> No <u>2</u>	35 <u> </u>
<u>If "yes" to 1,3,4 or 5</u>	
Do you have any such illness at present?	
Yes <u>1</u> No <u>2</u> N.A. <u>9</u>	36 <u> </u>

(6)

Data Column		Code Column
<u>ADDITIONAL ALLERGY HISTORY</u>		
1. Have you ever had atopic dermatitis, by which I mean a scaling rash that occurs in elbow creases, behind the knees and/or sometimes behind the ears?	Yes <u>1</u> No <u>2</u>	37 <u> </u>
2. Have you ever had urticaria, by which I mean swollen red spots on the skin which may or may not be itchy?	Yes <u>1</u> No <u>2</u>	38 <u> </u>
<u>If "yes" to 1 or 2</u>		
3. Do you have either such illness at present?	Yes <u>1</u> No <u>2</u> N.A. <u>9</u>	39 <u> </u>
4. Have you had more than 2 head colds each year for some time?	Yes <u>1</u> No <u>2</u>	40 <u> </u>
<u>If "yes" to 4</u>		
5. When you have a head cold, do you have runny, stuffy or itchy nose and/or sneezing for several days at a time?	Yes <u>1</u> No <u>2</u> N.A. <u>9</u>	41 <u> </u>
6. Do any members of your immediate family (mother, father, brothers, sisters) have any of the allergies I have mentioned: (a) asthma (attacks of shortness of breath with wheezing); (b) hay fever; sinus trouble; post nasal drip; a runny, stuffy or itchy nose and/or sneezing for several days at a time occurring at certain times of the year; (c) atopic dermatitis or (d) urticaria?	Yes <u>1</u> No <u>2</u>	42 <u> </u>

APPENDIX A

(7)

Data Column	Code Column
<u>If "yes" to 6</u>	
7. Which family member and what type allergy?	
Mother <u>1</u>	45 <u> </u>
Allergy: a <u>1</u> b <u>2</u> c <u>3</u> d <u>4</u>	46 <u> </u>
Father <u>2</u>	50 <u> </u>
Allergy: a <u>1</u> b <u>2</u> c <u>3</u> d <u>4</u>	51 <u> </u>
Sister <u>3</u>	55 <u> </u>
Allergy: a <u>1</u> b <u>2</u> c <u>3</u> d <u>4</u>	56 <u> </u>
Brother <u>4</u>	60 <u> </u>
Allergy: a <u>1</u> b <u>2</u> c <u>3</u> d <u>4</u>	61 <u> </u>

SMOKING

1. Do you now smoke cigarettes:	regularly	<u>1</u>	1-4 <u> </u>
	occasionally	<u>2</u>	
	(usually less than 1/day)		
	never	<u>3</u>	5 <u> </u>

If "regularly" now:

2. Do you inhale?	Yes <u>1</u> No <u>2</u> N.A. <u>9</u>	6 <u> </u>
3. Do you smoke cigarettes:	with filters <u>1</u>	
	without filters <u>2</u>	
	both with and without filters <u>3</u>	
	N.A. <u>9</u>	7 <u> </u>
4. How many cigarettes do you usually smoke each day at the present time?	<u> </u> <u> </u> N.A. <u>9</u> <u>9</u>	8-9 <u> </u>
5. How old were you when you began to smoke cigarettes?	<u> </u> <u> </u> N.A. <u>9</u> <u>9</u>	10-11 <u> </u>
6. What is the usual number you have smoked per day since you began to smoke?	<u> </u> <u> </u> N.A. <u>9</u> <u>9</u>	12-13 <u> </u>

APPENDIX A

(8)

Data Column	Code Column
<u>If "occasionally" or "never" now:</u>	
7. If you do not smoke cigarettes now, did you ever smoke them:	
<div> <div>regularly</div> <div>occasionally</div> <div>(usually less than 1 per day)</div> <div>never</div> <div>N.A.</div> </div> <div> <div><u>1</u></div> <div><u>2</u></div> <div><u>3</u></div> <div><u>9</u></div> </div>	14
<u>If "regularly"</u>	
8. What was the usual number of cigarettes you smoked per day?	
<div> <div>_____</div> <div>N.A.</div> <div><u>9</u></div> </div>	15-16
9. Did you inhale?	
<div> <div>Yes <u>1</u></div> <div>No <u>2</u></div> <div>N.A. <u>9</u></div> </div>	17
10. How old were you when you began to smoke cigarettes?	
<div> <div>_____</div> <div>N.A.</div> <div><u>9</u></div> <div><u>9</u></div> </div>	18-19
11. How old were you when you stopped smoking cigarettes regularly?	
<div> <div>_____</div> <div>N.A.</div> <div><u>9</u></div> <div><u>9</u></div> </div>	20-21
12. Were you influenced to stop smoking because you had a cough, wheezing or shortness of breath?	
<div> <div>Yes <u>1</u></div> <div>No <u>2</u></div> <div>N.A. <u>9</u></div> </div>	22
13. Do you now smoke pipes or cigars:	
<div> <div>regularly</div> <div>occasionally</div> <div>(usually less than 1 per day)</div> <div>never</div> </div> <div> <div><u>1</u></div> <div><u>2</u></div> <div><u>3</u></div> </div>	23
<u>If "regularly" now</u>	

APPENDIX A

(9)

Data Column	Code Column
14. How many pipefuls or cigars do you usually smoke each day?	
_____ N.A. <u>9</u> <u>9</u>	24-25 _____
15. How old were you when you first smoked pipes or cigars?	
_____ N.A. <u>9</u> <u>9</u>	26-27 _____
16. Do you usually inhale when you smoke either pipes or cigars?	
Yes <u>1</u> No <u>2</u> N.A. <u>9</u>	28 _____
<u>If "occasionally" or "never" now:</u>	
17. If you do not smoke cigars or pipes now, did you ever smoke them:	
regularly _____	<u>1</u>
occasionally _____	<u>2</u>
(usually less than 1 per day)	
never _____	<u>3</u>
N.A. _____	<u>9</u>
	29 _____
<u>If "regularly"</u>	
18. How many pipefuls or cigars did you usually smoke each day?	
_____ N.A. <u>9</u> <u>9</u>	30-31 _____
19. How old were you when you first smoked pipes or cigars?	
_____ N.A. <u>9</u> <u>9</u>	32-33 _____
20. How old were you when you stopped smoking pipes or cigars?	
_____ N.A. <u>9</u> <u>9</u>	34-35 _____

APPENDIX A

(10)

Data Column

Code Column

21. Did you usually inhale when you smoked either pipes or cigars?

___ N.A. 9 36 ___

EXPOSURE INFORMATION

22. Have you been off work for more than 3 weeks in the last 6 months?

Yes 1 No 2

If "yes" to 22:

23. For how many weeks? _____

24. What is your complete job title? _____
Study Classification

25. How frequently do you notice being exposed to the following gases?

	Frequency (Per week)	Duration (Minutes)
(a) Ammonia?	_____	_____
(b) TDI?	_____	_____
(c) Phosgene?	_____	_____
(d) Chlorine?	_____	_____
(e) Residue?	_____	_____

APPENDIX A

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26. Interviewer: _____ Schedule Code 3

SYMPTOM CLASSIFICATIONS

Bronchitis

Current Bronchitis	1 in cc 5 <u>or</u> 6 and
Usual cough and phlegm for	1 in cc 7 <u>and</u>
more than 3 months per year	1 in cc 9 <u>or</u> 10 <u>and</u>
	1 in cc 11

Chronic Bronchitis	Current bronchitis <u>and</u>
Current bronchitis for two	2 <u>or</u> 3 in cc 8 <u>and</u>
or more years	2 <u>or</u> 3 in cc 12

Lower Respiratory Symptoms	1 in cc 5 <u>or</u> 6 <u>or</u> 9
Cough, phlegm, wheezing,	<u>or</u> 10 <u>or</u> 13 <u>or</u> 17
SOB with wheezing, or SOB	<u>or</u> 19
when walking with other of	
own age	

Upper Respiratory Symptoms	1 in cc 32 <u>or</u> 36
Drip at back of nose,	
hay fever, or current	
sinus trouble	

Dyspnea	
Grade 1	2 in cc 18 <u>and</u> 19
Grade 2	1 in cc 18 <u>and</u>
	1 in cc 19
	2 in cc 18 <u>and</u> 19

Respiratory Atopy	1 in cc 14 <u>or</u> 33
Ever had asthma or hay	<u>or</u> 34
fever or any trouble	
around grass, pollen, etc.	

Dermal Atopy	1 in cc 37 <u>or</u> 38 <u>and</u>
Ever had eczema or hives,	1 in cc 42
and a positive family	
history of asthma or hay fever	

APPENDIX A

(12)

SYMPTOM CLASSIFICATION

Atopy	Either dermal or respiratory atopy	either of the above
Smoking		
Current Cigarette		1 in cc 5
Ex-Cigarette		2 <u>or</u> 3 in cc 5 <u>and</u>
Pipe/Cigar		1 in cc 14
		2 <u>or</u> 3 in cc 5 <u>and</u>
Never Smoker		1 in cc 23 <u>or</u> cc 29
		2 <u>or</u> 3 in cc 5 <u>and</u>
		2 <u>or</u> 3 in cc 23

A P P E N D I X B

TDI PLANT, B-451
TOLUENE DIISOCYANATE
POTENTIAL FOR EXPOSURE - ORDINAL RANKING*

I. OFFICE & SUPERVISORY PERSONNEL - LOW POTENTIAL

Production Superintendent
Assistant Production Superintendent
Production Supervisor
Sr. Production Engineer
Economic Evaluation Specialist
Shipping Coordinator
Sr. Computer Technician
Sr. Clerk Typist
Safety & Training Coordinator
Control A Operator
Sr. Parts Assistant
Equipment Technician

II. ENGINEERING, LAB AND MAINTENANCE CRAFT PERSONNEL -
MODERATE POTENTIAL

Production Engineer
Engineer
Production Foreman
Sr. Production Chemist
Sr. Lab Assistant
Chemical Assistant
Control C - Lab
Instrument Technologist
Instrument Technician
Electrician

III. PRODUCTION & MAINTENANCE PERSONNEL - HIGH POTENTIAL

Foreman
Loading Foreman
Rotating Shift Foreman
Control C - Outside
Control A - SRO
Class I Operators
Maintenance Foreman
Maintenance Technician
Machinists
Pipefitters

*These rankings are based on job tasks and amount of time spent in process areas.

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